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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/177,427
Filing Date: October 22, 1998
Appellant(s): LUKAS ET AL.

Kent H. Cheng
Reg. No. 33,849
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed July 14, 2005 appealing from the Office action mailed October 04, 2004.

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(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

CA 2,068,366	MORELLA et al.	11-1992
5,635,200	DOUGLAS et al.	06-1997
5,707,646	YAJIMA et al.	01-1998
4,808,411	LU et al.	02-1989

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

Claims 16-25 and 27-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morella et al. (CA 2068366) in view of Douglas et al. (USPN 5635200).

The instant invention is directed toward a formulation comprising particles having a core element containing one or more pharmaceutically active compounds and a substantially continuous polymeric coating thereon, wherein the polymer coating comprises less than 23% of the formulation, wherein said core has an aspect ratio of less than 3 and further wherein no more than 25% of the particles are less than 25 micrometers and no more than 2% of the particles are over 250 micrometers.

Morella et al. teach particles comprising a core containing at least one pharmaceutically active ingredient with a continuous coating on the core (abstract) for the purpose of producing a taste-masked free flowing powder. The coating comprises about 10-80% of the formulation (page 4, lines 15-23). The particle size of the core is about 0.1-250 microns, more preferably about 35-125 microns (page 4, line 38-page 5, line 4). The coating thickness is about 0.005-25 microns (page 5, lines 5-10). For paracetamol as the pharmaceutically active ingredient, see page 5, line 16. For ethyl cellulose as the coating agent, see page 8, lines 21-27. At page 13, lines 1-23, Morella et al. teach a process of making the particles comprising suspending or dispersing the pharmaceutically active ingredient in the coating solution and spray drying the suspension. See also example 1 at page 17, line 30-page 18, which teaches spray-drying a solution of ethylcellulose and paracetamol. The powder exhibited taste masking and sustained release of paracetamol. The reference fails to exemplify an aspect ratio of less than 3 and a spherical shape, wherein a spherical particle has an aspect ratio of 1.

While the aspect ratio is not explicitly taught, it is respectfully pointed out that Morella et al. doe teach an aspect ratio of less than 3. Since the aspect ratio is a measure of the length compared to the breadth and since Morella et al. teach 0.1-250 microns as the particle size and 0.005-25 microns as the thickness, it is respectfully pointed out that an aspect ratio of less than 3 is within the range taught by Morella et al.

Douglas et al. teach taste-masking compositions of ranitidine. It is taught that the preferred form of the particles is spherical because the presence of irregular shaped

particles reduces the effectiveness of subsequent overcoating procedures in masking the bitter taste of the active ingredient. Douglas et al. teach particles the same size range as those taught by Morella et al. See abstract, col. 5, lines 8-15.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to exemplify the microcapsules of Morella et al. as having an aspect ratio of 1 (a.k.a. a spherical shape), as taught by Douglas et al., because of an expectation of achieving a product that most effectively masks the bitter taste of paracetamol or another active ingredient.

Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Morella et al. and Douglas et al. as applied to claims 16-25 and 27-30 above, and further in view of either Lu et al. (USPN 4808411) or Yajima et al. (USPN 5707646).

Morella et al. and Douglas et al. apply as disclosed above. The references lack a teaching of clarithromycin.

Lu et al and Yajima et al. both teach that clarithromycin, an antibiotic, has a bitter tasted and is suitable for administration in particles that contain a polymer coating in order to provide sustained release and taste-masking. See col. 4, lines 24-27 and lines 57-61 of Lu et al.; and col. 2, line 25-col. 4, line 15 of Yajima et al.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to teach clarithromycin, as taught by Lu et al. and Yajima et al., as one of the active agents of the combined references because of the expectation of achieving a pharmaceutically acceptable formulation of clarithromycin that is effective in

masking its bitter taste and because Morella et al. teach that the pharmaceutically active ingredient may be any compound which may be utilized in taste-masked, sustained/delayed release treatment.

(10) Response to Argument

Applicant argues on page 5 of the appeal brief filed July 14, 2005, "In view of [the] extensive list of parameters [set forth by Morella et al.], it is submitted that while the reference may use broad language to describe the wt. % of the coating, the Examiner must consider the entire reference, and particularly the release rates of the drug over time." This argument is not persuasive because Morella et al. specifically set forth that the coating may be 10-80% of the formulation. Applicant has claimed a range that significantly overlaps with the teachings of Morella et al. Furthermore, Example 5 of Morella et al. illustrates a formulation wherein the coating comprises about 28% of the formulation. Accordingly, it would have been obvious to one of ordinary skill in the art to utilize the full range of coating percentages taught to be useful by Morella et al., particularly those near the 28% exemplified (i.e. those in the low 20's). It is also noted that it has been established that consideration of a reference is not limited to the preferred embodiments or working examples, but extends to the entire disclosure for what it fairly teaches, when viewed in light of the admitted knowledge in the art, to a person of ordinary skill in the art. *In re Boe*, 355 F.2d 961, 148 USPQ 507 (CCPA 1966); *In re Lamberti*, 545 F.2d 747, 19USPQ 279 (CCPA 1976); *In re Fracalossi*, 681

F.2d 792, 215 USPQ 569 (CCPA 1982); *In re Kaslow*, 707 F.2d 1366, 217 USPQ 1089 (Fed. Cir. 1983).

Applicant argues on pages 5-6 of the appeal brief filed July 14, 2005 that the "upper limit in release rate [of Morella et al.] would cover unacceptable release rates necessary for a sustained release formulation." Applicant's arguments are directed to the 30% release rate over 40 minutes of Example 1 and the 18% release rate over 40 minutes of Example 5. These arguments are not persuasive because there are no sustained release parameters set forth by the claims. The only limitation directed thereto is that the compositions "provide sustained release." Whether or not the sustained release parameters are unacceptable for a particular application, commercial viability, etc. is not relevant because the claims simply state that the composition must provide sustained release. It is clear, given the teachings of Examples 1 and 5, that the teachings of Morella et al. meet this limitation, as set forth in the claims as written. After 40 minutes, the composition of Example 1 has release 30% of the active ingredient and the composition of Example 5 has released only 18% of the active ingredient. If Examiner were to conclude that the release rates set forth in the prior art are insufficient to meet the limitations of the broadly claimed "sustained release", then the limitation could be set arbitrarily and would be indefinite. Lacking any specific dissolution and/or release parameters, the boundary between what constitutes sustained release and what does not would be vague and indeterminate to the skilled artisan. It would, in essence, be a judgement called made, individually, by each artisan. Furthermore, it is noted that Morella et al. specifically state that the coatings therein "may provide the

pharmaceutical ingredient with for example a sustained release profile ...". Thus, the inventors of Morella et al. anticipated that the formulations disclosed therein would have sustained release characteristics.

Applicant argues page 6 of the appeal brief filed July 14, 2005, "While the Examiner may be relying on Douglas only for the discussion of the aspect ratio or physical shape of the particles used by Douglas, it is submitted that the command of 35 U.S.C. § 103 requires that the entirety of the reference be considered. In this regard, it should be noted that Douglas provides absolutely no information as to the dissolution characteristics of his dosage form." This argument is not persuasive because it is Examiner's position that Morella et al. has set forth adequate disclosure to establish that the compositions therein would provide sustained release, as set forth by the claims. Furthermore, Applicant's arguments that Douglas et al. does not have a coating weight of 23 weight percent or less is not persuasive. Douglas et al. unequivocally state, "The preferred shape of the particles so formed is spherical. The presence of irregular shaped particles reduces the effectiveness of subsequent overcoating procedures in masking the bitter taste of the drug." See col. 5, lines 9-13. There is no indication that the benefits gained from the spherical shape are dependent on the amount of coating subsequently utilized. Accordingly, the one of ordinary skill in the art would have understood that a spherical shape would increase the taste-masking characteristic of a subsequently coated particle. Furthermore, it is noted that a particle comprising an aspect ratio of less than 3 is within the range set forth by Morella et al. Douglas is

simply utilized to emphasize that it is known in the art that the use of spherical particles is preferable when pertaining to taste masking formulations.

Applicant argues page 7 of the appeal brief filed July 14, 2005, "neither [Morella et al.] nor Douglas provides any motivation for one of ordinary skill in the art to combine the references so as to render obvious the presently claimed invention." This argument is not persuasive because Douglas et al. clearly establishes that the use of spherical particles is preferred for maximizing the masking of bitter tasting drugs. Applicant argues that there would be "no motivation to further modify the process described in [Morella et al.] with the disclosure of Douglas to further improve taste masking." This argument is not persuasive because if the target is a formulation with an effective taste masking characteristic, one would be motivated to combine two methods wherein each method is known to be individually useful for taste-masking, in order to maximize the taste-masking characteristic of the formulation. Furthermore, it is noted that the claims comprise the open language of "comprising". Thus, any discussion with regard to the presence or lack of an overcoating is irrelevant to the pending claims because the claims do not preclude an overcoating.

For the reasons set forth above, Examiner does not agree with Applicant's assertion that the combination of Morella et al. and Douglas et al. amounts to an "obvious to try" standard.

Applicant's arguments on page 9 of the appeal brief filed July 14, 2005 that Yajima et al. and Lu et al. are not relevant because they do not teach the relevant coating weight percentage. This argument is not persuasive because Examiner is not

relying on Yajima et al. or Lu et al. in order to determine the weight percentage of the coating material, but that it would have been obvious to prepare a formulation wherein clarithromycin was encapsulated by the coating material. Applicant next argues that Yajima et al. and Lu et al. cannot be combined with Morella et al. and Douglas et al. because the processes of preparing the compositions therein are not identical to those of the instant invention. This argument is not persuasive because Examiner is not relying on Yajima et al. and Lu et al. in order to render a method of making a given formulation obvious. Examiner is relying on Yajima et al. and Lu et al. to show that it is desirable to mask the taste of and achieve sustained release of clarithromycin. Furthermore, Yajima et al. and Lu et al. teach that clarithromycin is suitable for administration in particles that contain a polymer coating. Therefore, it is Examiner's position that these references are of an analogous art to both Morella et al. and Douglas et al. Morella et al. states that the each microcapsule of the invention taught therein includes an effective amount of a core element including at least one pharmaceutically active ingredient. Morella et al. further states that the purpose of the microcapsule is to mask the taste of and provide a reduced dissolution profile of the encapsulated material. See Abstract. Accordingly, it is Examiner's position that it would have been obvious to one of ordinary skill in the art to encapsulate a pharmaceutical in a manner rendered obvious by the combination of Morella et al. and Douglas et al. wherein it would have been desirable to provide sustained release and taste masking of said pharmaceutical. Yajima et al. and Lu et al. teach that clarithromycin is such a pharmaceutical.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Gregory W Mitchell
Examiner
Art Unit 1617

Conferees:

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